Remarks

Claims 1-11 are pending in this application. Claim 12-15 were previously cancelled. Claims 3 and 5 are currently withdrawn. Claim 1 has been amended to include the limitation that the interfering factor is a drug. This amendment finds support at page 2, second paragraph of the specification. Claim 1 also is amended to more clearly define which portion of the AT binding factor is being determined at each step of the claimed process. To the extent the claim is amended for clarity, those amendments are not intended to limit the scope of the claim.

Rejections Under 35 U.S.C. § 112, First Paragraph

The rejection of the claims under consideration for failing to comply with the written description requirement is respectfully traversed, because the specification describes the claimed subject matter in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The present invention is a method of determining AT in a sample that may contain an interfering factor. The invention lies in the use of an excess of AT binding partner, such that a portion of the AT binding partner interacts with the interfering factor under conditions in which the AT binding partner does not interact with AT so that the interfering factor no longer interferes with the subsequent determinations of the remaining free AT binding partner both before and after it has reacted with the AT, the difference between the two determinations being indicative of the amount of AT in the sample.

The Examiner has rejected the claims on the basis that the "claimed reagents" and "interfering factor" are not adequately described in the specification. At the outset, it should be noted that it is not the reagents themselves that are claimed, but the novel *sequence of steps* for using the reagents to determine AT. Any reagents that perform the stated functions, whether now known or to be discovered in the future, will be understood by those skilled in the art to be suitable for the claimed sequence of steps of the present invention. As stated in the MPEP, "The absence of definitions or details for well-established terms or procedures should not be the basis of a rejection under 35 U.S.C. 112, para. 1, for lack of adequate written description." In this case, as will be shown, such suitable reagents are well known in the art.

With regard to the reagent R1 which contains the AT binding partner, the Examiner has stated that, "Absent a disclosed correlation between structure and function, one skilled in the art would not envisage possession of the genus of R1 reagents based on the definition of the two species thrombin and factor Xa." But the applicant is not claiming all reagents R1, i.e., all binding partners of AT, per se. Rather, applicant is claiming the *use* of such a reagent R1 in a novel sequence of steps to perform an analysis of AT. The applicant does not have to be in possession of all possible AT binding partners in order to be in possession of the novel sequence of steps of the invention.

With respect to particular biological molecules, as explained by the Federal Circuit, "(1) examples are not necessary to support the adequacy of a written description; (2) the written description standard may be met ... even where actual reduction to practice of an invention is absent; and (3) there is no per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure." *Falkner v. Inglis*, 448 F.3d 1357, 1366, 79 USPQ2d 1001, 1007 (Fed. Cir. 2006). The MPEP further points out that additionally, unique cleavage by particular enzymes, isoelectric points of fragments, detailed restriction enzyme maps, a comparison of enzymatic activities, or antibody cross-reactivity may be sufficient to show possession of the claimed invention to one of skill in the art. See *Lockwood*, 107 F.3d 1565,1572, 41 USPQ2d 1961,1966 ("written description" requirement may be satisfied by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention"). MPEP § 2163.II.A.E.a.

In this case, those skilled in the art of AT determinations would understand the scope of the reagents R1, R2, and R3 that would be suitable for use in the novel sequence of steps of the claimed invention. In addition to the art already of record in this case, applicant refers to the art submitted herewith, some of which is cited in the specification at paragraphs [0003] and [0004]. (Applicant expects to submit full copies of these references with a Supplemental Information Disclosure Statement in the near future; partial copies are submitted herewith for preliminary review.) Lill et al. discloses a detailed description of AT determination methods, including the various reagents that can be used at each step. Chromogenic substrates are discussed in the Fareed et al., and Abildgaard et al references. These references show that various reagents suitable for carrying out the novel claimed method were known in the art at the time of the invention. The particular structural characteristics of any of the reagents are not critical to the

ability of one skilled in the art to practice the inventive method of determining AT. Those skilled in the art, upon reading the disclosure of the present specification and the claimed sequence of steps, will be able to select known reagents that will perform the recited functions in the sequence of steps to be able to practice the claimed invention.

For example, with regard to reagent R2 which used is used to determine the binding partner of R1, applicant is not "attempting to describe an unknown by reference to another unknown," as the Examiner suggests. One skilled in the art, upon selecting an AT binding partner for reagent R1, will be sufficiently skilled to choose a reagent R2 that will allow the determination of that selected AT binding partner. Those skilled in the art similarly will know how to select reagents for R3, and an additional AT binding partner of claim 10.

Not everything necessary to practice the invention need be disclosed. In fact, what is well-known is best omitted. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991). All that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art. See, e.g., *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). MPEP 2164.08. In this case, one skilled in the art of AT determination will have sufficient knowledge to choose reagents to practice the sequence of steps that is the subject matter of the invention. Accordingly, the written description is adequate.

Rejections Under 35 U.S.C. § 112, Second Paragraph

The claims were rejected as indefinite under the second paragraph of 35 U.S.C. 112 because in claim 1 the recitation of "the free fraction of the AT binding partner" lacked antecedent basis, and because step (b) was believed to be indefinite. It is respectfully submitted that the present amendments to claim 1 correct these deficiencies, and it is respectfully requested that this ground of rejection be withdrawn.

Rejections Under 35 U.S.C. § 103

The rejection of claims 1-2, 4, 6-7, and 11 as obvious over Plattner et al. in view of Furatu, Morris et al, and Akhavan-Tafti et al. is respectfully traversed.

One aspect of the invention lies in the surprising discovery that it is possible to conduct two reliable determinations of free fractions of AT binding partner successively in one and the same sample. Yet, the skilled person upon reading Plattner et al., would have expected that a

reliable comparison between the first and second determinations of free fractions of AT binding partner would not have been possible, due to the addition of the R3 reagent between the first and second determinations.

As the Examiner correctly notes, Plattner et al. differs from the claimed invention in that it fails to specifically teach conducting the two measurements of the same substance at different times in a single reaction mixture. The Furatu reference does not teach the analysis of a single substance by two separate measurements in a single reaction mixture. Instead, Furatu in the paragraph spanning pages 3-4, teaches the analysis of a "first analysis item," then adding a reagent to measure a "second analysis item," the calculation of the concentration of the "second analysis item" being corrected to account for the amount of reagent added. This does not teach comparative analyses of any single analyte, and certainly not of an AT binding partner under different reaction conditions to determine AT. The Morris reference teaches repetitive tests on the same sample over a period of time to confirm the presence of a disease. Morris does not teach taking the difference between any two tests to determine a particular analyte. The Akhvan-Tafti reference also teaches taking the measurements of two different analytes at a single time, not using the difference between two measurements at different times and under different condition on the same sample to determine a single analyte.

The examiner's open-ended statement, "it would have been obvious to use known techniques to improve upon known methods in which multiple measurements are performed, such as those of Plattner et al." (Office Action page 10) does not state how the references would be combined. In fact, the references which teach different measurements of different analytes cannot be combined to give or render obvious the claimed sequence of steps used to measure AT. The Examiner states that these references teach the desirability of performing multiple measurements sequentially on a single sample, instead of in parallel on multiple samples (Office Action, p. 14). But none of them teach or suggest performing measurements of the same substance under different conditions and comparing the measurements in order to obtain a determination of an analyte, which is the essence of the present invention.

The Examiner's suggestion that one skilled in the art would have employed "creative steps" is belied by a presentation at the 2008 GTH Congress (Congress of Gesellschaft für Thrombose-und-Hämostaseforschung, held February 20-23, 2008, Wiesbaden, Germany), a meeting of those skilled in the art. The Hickey monograph shows that the problem of the

presence of the drug Leprudin as an interfering factor in determinations of AT still had not been solved. If employing the "creative step" of the present invention would have been obvious to those skilled in the art, those steps would have been so employed by the time of the GTH 2008 congress. The "creative step" that the Examiner dismisses as obvious is in fact one that has not yet been employed by others to solve this long-recognized need in the art.

As claim 1 is non-obvious, the remaining claims dependent from claim 1 also are non-obvious.

In view of the foregoing, a notice of allowance is respectfully requested.

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